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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/817,560	04/02/2004	Stephen J. Benkovic	7418/91839	3809

24628 7590 03/28/2007
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EXAMINER

STAPLES, MARK

ART UNIT	PAPER NUMBER
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1637

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/817,560	Applicant(s) BENKOVIC ET AL.	
	Examiner Mark Staples	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/21/2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 33-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33-37 is/are rejected.
- 7) ☒ Claim(s) 33 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants' amendment of claim 33 in the paper filed on 12/21/2006 is acknowledged.

Claims 33-37 are pending and at issue.

Applicants' arguments filed on 12/21/2006 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections and Rejections that are Withdrawn / Moot

2. The objection to the abstract is withdrawn in light of the Applicant's amendment of the abstract.

3. The objection to the title is withdrawn in light of the Applicant's amendment of the title. However, a new objection to the title is made, please see below.

Claim Rejections Withdrawn - 35 USC § 112 Second Paragraph

4. The rejections of claims 33-37 under 35 USC § 112 Second Paragraph are withdrawn in light of the Applicant's amendment of claim 33 to recite how the library of the preamble is formed.

New Rejections and Objections Necessitated by Amendment

5. Claim 33 is objected to because of the following informalities: the apparent omission of the word "stranded" in the phrase "the first double [sic, *stranded* is omitted] DNA" found in line 6 of the claim. Appropriate correction is required.
6. The new title is objected to for repetition of the word "FOR". Appropriate correction is required.

New Claim Rejections - 35 USC § 112 Second Paragraph

7. Claims 33-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "partial" in claim 33 is a relative term which renders the claim indefinite. The term "partial" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Thus, the amount of homology or non-homology in claim 33 is rendered indefinite by use of the term "partial". Due to independent claim 33 being indefinite and with no clarification in subsequent claims of "partial", dependent claims 34-37 are also indefinite.

The term "partial homology or non-homology" in claim 33 is indefinite as it has at least two different interpretations. These are: (1) where there is partial homology or where there is non-homology and (2) where there is partial homology or where there is partial non-homology. The later interpretation is redundant as partial homology is partial

non-homology. Due to this indefiniteness and potential redundancy, claims 33-37 are indefinite.

Rejections that are Maintained

Claim Rejections Maintained - 35 USC § 102(b)

8. It is noted that the specification of the instant application does not provide definitions of either "plurality", "random sizes", or "library". The claims are then given the broadest reasonable interpretations with respect to these elements. More than one of a thing has and is interpreted as being a "plurality".

At least two different fragments being formed without definite aim is the interpretation given to "random fragments". In regards to incubating DNA with exonuclease activity to from a plurality of random sizes, Fangman gives the following definition of exonuclease:

"An enzyme that cleaves nucleotides one at a time from an end of a polynucleotide chain"

" exonuclease." GENETICS 372 Winter 2000. W. Fangman,
retrieved 17 Mar. 2007

<<http://depts.washington.edu/~genetics/courses/genet372/w2000Terms.html> >.

And the property of an exonuclease to form libraries is evidenced by Ostermeier et al. (1999):

"Libraries of incremental truncations [random DNA sizes] from the C terminus of the purN[1-144] gene fragment and from the N terminus of the

purN[63–212] gene fragment were created by using Exo III [an exonuclease]"
(see last sentence in first column on page 3563).

Thus exonuclease activity has the property of no definite aim in regards to what is on the end of the polynucleotide. The above definition and evidence and the lack of a definition in the specification, much less a definition which is further limiting than these two citations, the formation of random sizes in claim 33 is an inherent property of exonuclease activity. In other words, simply incubating DNA with an enzyme with exonuclease activity will result in random sizes, as there is no aim in the exonuclease activity. Exonuclease activity cleaves any nucleotide, one at time from an end of a polynucleotide. Each of the three prior art references below teach methods using exonucleases without any further limitation and thus inherent in the methods of these three reference is the formation of DNA of random sizes.

A collection or two of more DNA sequences/fragments is interpreted to be a "library" in the context of the claim language. It is also noted that specification directs the reader to Figure 1 for depiction of the creation of library. In this figure is shown the inherent features formed through a Holliday junction which is three fragments of DNA (see Figure 1, next to last depiction in which two gaps define three fragments of DNA, a middle fragment and two fragment each on opposite sides of the middle fragment). Thus the three prior art references given below, in teaching methods using Holliday junctions, inherently form through these methods the library, as recited in the instant claim 33.

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9. Applicant's arguments in the response filed on 12/21/2006, with respect to the rejection(s) of claim(s) 33-37 under 102(b) as being anticipated by Mosig (1998) have been fully considered and are not persuasive.

The rejection of claim 33 is maintained. Applicant does not argue against the teachings of Mosig in regards to dependent claims 34-37 and thus these rejections are also maintained.

Contrary to Applicant's arguments in regards to claim 33, Mosig does teach: "Regions of ssDNA . . . can be generated in several ways; by nucleases, helicases, or by the process of DNA replication (Figure 2). . . . An exonuclease encoded by, or controlled by these genes can generate partially ssDNA at ends or by converting ssDNA nicks to gaps" (see p. 387, 2nd 3rd, and 4th sentences) and continues by teaching: "Single-stranded DNA segments [that is a plurality] can be formed by partial nucleolytic degradation (a,b)"; where "(a,b)" are illustrations of double stranded DNA which leads to the single stranded segments (note the plural of segments, see Figure 2 and legend therein). And it was known in the art that endonuclease digestion results in random sizes of DNA fragments simply by not proceeding to completion by forming libraries of incremental truncations. And as noted above this is evidenced by Ostermeier et al. (1999):

"Libraries of incremental truncations [random DNA sizes] from the C terminus of the purN[1-144] gene fragment and from the N terminus of the purN[63-212] gene fragment were created by using Exo III [an exonuclease]" (see last sentence in first column on page 3563).

Also contrary to Applicant's further arguments in regards to claim 33, Mosig teaches not just homologous recombination but "Single-stranded DNA invading a region of partial homology . . . "(see last sentence of the legend to Figure 5). In other words, Mosig teaches the claim 33 limitation of a "single stranded DNA regions, at least one of which has a region of partial homology".

In response to applicant's argument that "nowhere is the method as a whole taught", Mosig teaches all of the elements of the claims 33-37, therefore the rejections of these claims are maintained.

10. Applicant's arguments in the response filed on 12/21/2006, with respect to the rejection(s) of claim 33 under 35 U.S.C. 102(b) as being anticipated by Kowalczykowski (1994) have been fully considered and are not persuasive.

The basis for Applicant's argument is the indefinite claim limitation of "partial homology or non-homology". Due to this indefiniteness, it cannot be determined if Applicant's argument is applicable or not to the teachings of Kowalczykowski. It is however noted that some non-homology is inherently taught by Kowalczykowski as even homologous recombination only has to have some portion of the two sequences being homologous (other portions can be non-homologous) as known in the art and as evidenced by Bollag et al. (1989):

"The homology requirements of ECR [Extrachromosomal recombination, a type of homologous recombination, see Introduction on p. 240] were initially

addressed by measuring recombination frequency as a function of length of homology shared by two sequences" (see p. 203, 1st sentence of 1st paragraph).

In response to applicant's argument that "nowhere is the method as a whole taught", Kowalczykowski teaches all of the elements of the claim 33 and therefore the rejections of this claim is maintained.

11. Applicant's arguments in the response filed on 12/21/2006, with respect to the rejection(s) of claims 33–34 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by West (1992) have been fully considered and are not persuasive.

The rejection of claim 33 is maintained. Applicant does not argue against the teachings of West in regards to dependent claims 34 and 37 and thus these rejections are also maintained.

Contrary to Applicant's arguments in regards to claim 33, West does teach Holliday junctions, that is a plurality of junction.⁵

In response to applicant's argument that "nowhere is the method as a whole taught", West teaches all of the elements of the claims 33, 34, and 37, therefore the rejections of these claims are maintained.

Conclusion

12. Claims 33-37 are not free of the prior art.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

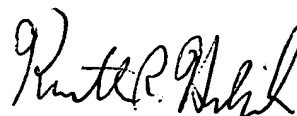
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples
Examiner
Art Unit 1637
March 16, 2007

MS


KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
3/21/07